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Dear Josh:

In thinking about phase variation in Salmonella, I come up with the following:

(1) Is there any evidence that the H_2 locus is bipartite with a separable "controlling element", which might work or not work when moved elsewhere?

(2) Are there any metabolic conditions which can alter the frequency of phase shifts? In other words, can the "controlling element" best be visualized at present as an autonomous factor whose on-off shifts are independent of any known metabolic variables? or not?

(3) I have been wondering about a formal analogy with the Paramecium antigens along the following lines: that the systems are basically the same, both involving [redacted] ultimately, at the working end, repression of all but one antigen-forming-site. If repressors are bipartite, with one component a direct gene product and the other a metabolite, then control of antigen formation might appear either genic or "cytoplasmic"(in the Paramecium sense) depending upon which was the limiting factor, i.e. rate-determining step. From [redacted] Beale's descriptions of the temperature-determined antigen series, [redacted] which is so very sluggish in its response, it would seem to me that the metabolic component might be rate-limiting, and consequently obscure the [redacted] role of a genetic element. (ie in a non-mutant system where the genetic factor is not segregating: present in both parents)

SAGER, R.

I've just read Tracy's analysis of the "new biology" in the PNAS, and to my consternation, I find that while I disagree with many of his specific points of analysis, I had reached some of the same conclusions. [redacted] Resistant as I am to band-wagons, I have been very much impressed with the usefulness of the repression framework. What to do with my non-chromosomal determinants? They are good band-wagon antidotes. Not fitting any of the current popular schema, I can only conclude that I must continue to work with them. I still think they represent a general and essential feature of cell heredity -- but at the moment I seem to be the only person in the world who thinks so, and it is somewhat uncomfortable.

I enjoyed visiting with you and Esther very much. Please let me know if you come east. I shall be here until Augugst, and after Sept. 15.

With affectionate regards, greetings, etc.

Ruth